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ORIGINAL RESEARCH

POST-OPERATIVE SPORT PARTICIPATION AND SATISFACTION WITH RETURN TO ACTIVITY AFTER MATRIX-INDUCED AUTOLOGOUS CHONDROCYTE IMPLANTATION IN THE KNEE

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ABSTRACT

Background: Returning to a satisfactory activity level is expected by patients after cartilage repair, and may define overall surgical success.

Purpose: To investigate: 1) the level and improvement in activity in patients at two years after matrix-induced autologous chondrocyte implantation (MACI), 2) what factors are associated with post-operative (and improvement in) activity level, and 3) whether patients are satisfied with their ability to participate in recreational and/or sporting activities.

Study Design: Prospective cohort.

Methods: One hundred and fifty patients that underwent MACI were included in this analysis (83 tibiofemoral and 67 patellofemoral). All patients completed the Tegner Activity Scale (TAS) and the Knee Injury and Osteoarthritis Outcome Score (KOOS) pre-surgery and at two years (range: 24-26 months) post-surgery, as well as a questionnaire evaluating satisfaction with their ability to return to recreational and sporting activities.

Results: The TAS significantly improved ($p < 0.001$) from 2.97 (SD 0.92, range 0-7) to 4.09 (SD 1.49, range 0-9), while the KOOS Sport significantly improved ($p < 0.0001$) from 27.5 (SD 23.1, range 0-95) to 61.1 (SD 27.3, range 0-100). Overall, 88 patients (59%) improved ≥1 point on the TAS, while 121 patients (81%) improved ≥10 points on the KOOS Sport, previously reported as the minimal detectable change for each. Patient age, duration of symptoms (DOS) and gender were associated with post-operative activity level, though body mass index (BMI), defect size and concomitant procedures were not. Overall, 128 patients (85%) were satisfied with their ability to return to recreational activities, with 99 (66%) satisfied with sport participation. The two-year TAS, and TAS improvement, were significantly associated with satisfaction in performing recreational activities (two-year TAS, rho = -0.42, $p < 0.0001$; TAS improvement, $r = -0.33$, $p < 0.0001$) and sport participation (two-year TAS, rho = -0.49, $p < 0.0001$; TAS improvement, $r = -0.37$, $p < 0.0001$).

Conclusions: The TAS and KOOS Sport significantly improved after MACI, though only 59% of patients improved ≥1 point on the TAS. Despite this, 85% and 66% of patients were satisfied with their ability to return to recreational activities and participate in sport, respectively. Age, DOS and gender were associated with activity, and overall these findings can be used to provide realistic activity expectations to patients undergoing MACI.

Level of Evidence: Level 3, prospective cohort study

Keywords: Chondral defect, clinical outcomes, matrix-induced autologous chondrocyte implantation, movement system, patient satisfaction, return to sport.

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INTRODUCTION

Matrix-induced autologous chondrocyte implantation (MACI) is a cartilage regenerative procedure that involves an initial cartilage biopsy, followed by isolation and cultivation of chondrocytes *ex-vivo*, seeding of cells onto a collagen membrane and subsequent re-implantation of the cell scaffold into the knee. MACI has demonstrated an ability to reduce pain and symptoms associated with full thickness cartilage defects.[1-6] However, while Zak et al.[7] reported that a reduction of symptoms is imperative, achieving a satisfactory post-operative activity level is often expected by the athletic patient,[8] and may well define the overall success of the surgery.[9]

A systematic review reported that the rate of return to sport (RTS) varied from 75-89% after a range of knee cartilage repair procedures (osteochondral autograft and allografts, chondrocyte implantation and microfracture).[10] A more recent meta-analysis by Krych et al.[11] also reported that overall 76% of patients RTS at mid-term follow up (mean 47 months) after cartilage restoration surgery. While published evidence is relatively scarce on this topic, particularly with respect to MACI, Zak et al.[7] reported that participation in regular sports similar to pre-injury recreational levels and intensity is possible for most patients following matrix-associated autologous chondrocyte transplantation (MACT). However, a range of factors may affect post-operative activity level (in addition to ongoing knee problems), including family and work commitments, as well as other musculoskeletal and health concerns, particularly in a community level patient cohort (as opposed to professional and elite athletes).

Given the limited research that exists on exactly what level of (and improvement in) activity MACI patients do attain after surgery, as well as what factors may affect post-operative activity and whether patients are indeed satisfied with their level of activity, this study sought to address these questions. The purpose of this study was to investigate: 1) the level of activity that a community level cohort of patients undergoing MACI attains at two years after surgery, 2) what factors are associated with post-operative activity level, as well as the improvement in activity level after surgery, and 3) whether patients are satisfied with their ability to participate in recreational and/or sporting activities. It was hypothesized that: 1) patient activity level would significantly improve following MACI, 2) certain factors (including defect location and size, gender, age) would be associated with the level of (and improvement in) post-operative activity level, and 3) a high percentage of patients would be satisfied with their ability to participate in recreational and/or sporting activities at two years following surgery.

METHODS

Patients

In this prospective study, 160 patients undergoing tibiofemoral (TF) or patellofemoral (PF) MACI were referred into a structured research program between July 2005 and April 2014, and followed for two years (range: 24-26 months) post-operatively. Patients were deemed suitable for MACI if they presented with symptomatic grade III/IV unipolar chondral lesions, assessed with the International Cartilage Repair Society (ICRS) classification system, were 15-65 years of age and deemed able to follow a structured rehabilitation program. All patients underwent pre-operative magnetic resonance imaging (MRI) to evaluate the location, size and severity of the chondral defect, as well as other soft tissue damage. MACI was contraindicated in the presence of ligamentous instability (unless it was to be addressed surgically at the time of MACI surgery), prior extensive meniscectomy (>1/3 meniscus), inflammatory arthritis and/or had varus/valgus lower limb mal-alignment (as indicated by > 3° TF anatomic angle). Joint mal-alignment was clinically assessed by the orthopaedic specialist, and long leg alignment radiographs (Maquet views) were ordered if the surgeon felt that further investigation was warranted. PF patients also underwent computed tomography (CT) imaging to assess the degree (if any) of patellofemoral knee joint mal-alignment. Patients underwent surgery by six orthopedic surgeons (with ≥8 years experience in orthopedic practice) operating out of five hospitals (four private and one public).

Of the 160 patients that underwent MACI surgery and were recruited, 10 patients could not be located for the two year clinical review, so were excluded from the analysis. Therefore, 150 patients (93.8%) were included, including 83 in the TF joint (63 medial femoral condyle; 20 lateral femoral condyle) and 67 in the PF joint (35 patella; 32 trochlea) (Table 1). Of the 150 patients, 92 patients (61.3%) had undergone prior surgery including arthroscopy (n = 88), microfracture (n = 4), partial meniscectomy (n = 61), anterior cruciate ligament (ACL) reconstruction (n = 8), extensor realignment (n = 4) and/or lateral release (n = 15). At the time of MACI, 40 patients (26.7%) underwent concomitant surgery including ACL reconstruction (n = 5), posterior cruciate ligament reconstruction (PCLR) (n = 3), partial meniscectomy (n = 10), high tibial osteotomy (n = 4) and combined lateral PF retinacular release and anteromedial tibial tubercle transfer (TTT) (n = 26). All PF realignment surgeries were undertaken in the PF MACI group. Ethics approval was obtained from the Hollywood Private Hospital Human Research Ethics Committee (HPH145), and the consent of all patients was obtained and their rights protected.

Knee Surgery

Initially, patients underwent arthroscopic knee surgery to harvest a sample of articular cartilage from a non weight bearing area of the knee. At this time, the chondral defect, together with meniscal and ligamentous integrity, were evaluated. The chondrocytes from the cartilage harvest were cultured for approximately six to eight weeks and seeded onto a type I/III collagen membrane (ACI-Maix Matricel GmbH, Germany). In a second stage surgery performed via open arthrotomy, the defect was prepared and the loaded membrane was fixed to the subchondral bone. On pre-operative CT imaging, 26 patients (all undergoing PF MACI) presented with lateralization of the tibial tuberosity >9mm, which was deemed an indication for concomitant lateral PF retinacular release and anteromedial TTT performed using the Heatley modification[12] of the Fulkerson technique,[13] in combination with MACI.

Post-operative Management

Early post-surgery, all patients (PF and TF MACI) underwent 0-30° continuous passive motion (within 12-24 hours) for a minimum of one hour daily; cryotherapy for edema control; ankle pump exercises; isometric quadriceps, hamstrings and gluteal contractions; practical education regarding proficient weight bearing (≤20% body weight), and education on how to fit their hinged knee brace (initially worn 24 hours

Table 1. *Patient demographics at the time of surgery, for both the tibiofemoral (TF) and patellofemoral (PF) patient cohorts.*

Variable		Measure	TF	PF
Patients		n	83	67
Defect Location		n	63 (MFC), 20 (LFC)	35 (patella), 32 (trochlea)
Gender (males / females)		n (%)	52 (62.7) / 31 (37.3)	43 (64.2) / 24 (35.8)
BMI		Mean (range)	26.6 (18.4-36.2)	26.3 (19.4–36.7)
DOS (y)		Mean (range)	8.4 (1–26)	7.3 (1–21)
Age (y)		Mean (range)	38.2 (15-62)	37.9 (20–65)
	15-20	n (%)	5 (6.0)	3 (4.5)
	21-30		20 (24.1)	17 (25.3)
	31-40		31 (37.4)	24 (35.8)
	41-50		20 (24.1)	16 (23.9)
	51-60		6 (7.2)	6 (9.0)
	61-65		1 (1.2)	1 (1.5)
Defect Size (cm^2)		Mean (range)	3.2 (0.7-10.0)	3.0 (0.7-12.2)
	≤1.0	n (%)	7 (8.4)	9 (13.4)
	1.1-2.0		18 (21.7)	14 (20.9)
	2.1-3.0		14 (16.9)	11 (16.4)
	3.1-4.0		13 (15.7)	6 (9.0)
	4.1-5.0		9 (10.8)	12 (17.9)
	≥5.1		22 (26.5)	15 (22.4)

MFC = medial femoral condyle; LFC = lateral femoral condyle; BMI = Body Mass Index; DOS = Duration of Symptoms.

per day, and progressed as per the recommendations in Table 2). All patients participated in an out-patient rehabilitation program over a 12-week period, with ongoing advice and education provided up until 12 months (and beyond) as required. Supervised by two primary therapists, rehabilitation over the period was undertaken by five therapists (Physiotherapists and Accredited Exercise Physiologists). An overview of the rehabilitation protocol followed is provided in Table 2. However, the progression of weight bearing, knee bracing and exercises differed depending on graft location (TF versus PF) and size, concomitant surgeries (i.e. ligament reconstruction, osteotomy etc.) and individual patient progression and load tolerance. Furthermore, while the exercise program consisted of a combination of supervised rehabilitation sessions (that became less frequent following the initial three months post-surgery) as well as home (and pool) based supplemental exercises, the frequency and dosage of each individual exercise differed based on the exercise (and recovery time that may be required) and individual patient progression and tolerance to the exercises.

Table 2. *Overview of rehabilitation undertaken by tibiofemoral (TF) and patellofemoral (PF) patients participating in the research program.*

Timeline	Rehabilitation Guidelines
Week 1-2	• WB: ≤ 20% BW • Ambulatory Aids: 2 crutches used at all times • Knee ROM: passive and active ROM restricted to 0-30° • Knee Bracing: hinged brace, 0-30° • Rehabilitation: ankle pump exercises, isometric contractions (of the quadriceps, hamstrings, adductor and gluteal musculature) and straight leg exercises (hip flexion, extension, abduction and adduction), passive and active knee flexion exercises, soft tissue massage therapy, patella mobilization, CPM and cryotherapy
Week 3-6	• WB: progress toward 60% BW (TF) and full WB (PF) • Ambulatory Aids : 1-2 crutches dictated by WB status • Knee ROM: progress toward 0-125° (TF and PF) • Knee Bracing: progress toward full permitted knee flexion (TF and PF) • Rehabilitation: continuation and progression (i.e. increasing load) of isometric/straight leg and passive/active knee flexion exercises, soft tissue massage therapy, patella mobilization, CPM as needed, cryotherapy. Inclusion of aquatic therapy exercises (including deep water forwards, backwards and sideways walking, heel raises, mini squats, straight leg hip flexion, extension, abduction & circumduction, knee flexion and extension, cycling, scissor kicks), heel raises, weighted isotonic hip flexion, extension, adduction and abduction, trunk strengthening (such as supine situps, weight supported isotonic trunk flexion), hamstring and calf stretches, recumbent cycling
Week 7-12	• WB: progress toward full WB as tolerated • Ambulatory Aids: 1 crutch as required until full WB achieved • Knee ROM: full active ROM • Knee Bracing: full knee flexion (brace removed from 7-12 weeks) • Rehabilitation: introduction of proprioceptive/balance activities (such as double and single limb standing exercises on stable and unstable surfaces), upright stationary cycling, walking, progression of resistance (such as weighted isotonic knee flexion exercises) and CKC (such as flexed and straight leg bridging, single limb heel raises) exercises, quadriceps and gluteal stretches
3-6 months	• Rehabilitation: introduction of rowing ergometry and elliptical trainers, OKC quadriceps-focused (such as terminal, progressing toward full range knee extension) and CKC (such as leg press, squats, lunges and step variations) exercises, initiation of plyometric and jump/land exercises relevant to the patient's individual activity goals
6-12 months	• Rehabilitation: gradual increase in difficulty/demands of proprioceptive/balance, and resistance during OKC and CKC exercises, plyometrics, introduction of agility drills relevant to patient's sport, return to competitive activity after 12 months

ROM = range of motion; BW = body weight; WB = weight bearing; CPM = continuous passive motion; CKC = closed kinetic chain; OKC = open kinetic chain.

Clinical Assessment

Firstly, the TAS[14] was employed pre-surgery and at two years post-surgery to grade current work and sporting activities. This reports on the patient's activity level on a 0-10 point scale, ranging from sick leave or disability (0 points) through to elite competitive sports (10 points). Patients selected one of the levels of participation that best described their current activity level. While the minimum detectable change (MDC) for the TAS has been reported as 1 point in patients with ACL injuries and meniscal lesions,[15,16] it has not been reported specifically for those with cartilage lesions or undergoing cartilage repair. Secondly, the Knee Injury and Osteoarthritis Outcome Score (KOOS) was employed in all patients. The KOOS is a knee specific questionnaire which includes five individual subscales: Pain, Symptoms, Activities of Daily Living (ADL), Sport and Recreation (Sport) and Knee Related Quality of Life (QOL).[17] Each of these five subscales is scored from 0 (worst) to 100 (best). The KOOS has proven valid, reliable and responsive to treatment following cartilage repair.[18] Specifically for this study, the KOOS Sport subscale was employed to evaluate the improvement in sport-related activities (i.e. running, jumping, turning/twisting, kneeling and squatting). While evidence is lacking to suggest an MDC for the KOOS Sport subscale in patients undergoing cartilage repair, an MDC of 10 points is commonly employed.[19]

Finally, at two years post-surgery a patient satisfaction questionnaire was employed, based on the Self-Administered Patient Satisfaction Scale (SAPSS) developed by Mahomed et al.,[20] though used previously for patients following MACI.[3,6,21] This was employed to investigate each patient's level of satisfaction with the MACI surgery overall, as well as their satisfaction with MACI in relieving knee pain, improving their ability to perform normal daily activities, improving their ability to return to recreational activities and improving their ability to participate in sport. A Likert response scale was employed with descriptors Very Satisfied, Somewhat Satisfied, Somewhat Dissatisfied and Very Dissatisfied.

Data and Statistical Analysis

Firstly, this study sought to investigate outcomes in community level patients undergoing MACI concomitantly with a range of other surgical procedures (26.7% of patients in this sample). However, it is acknowledged that these adjunctive procedures could influence post-operative activity and associated satisfaction so t-tests were employed to investigate differences in patient variables (age, BMI, defect size and duration of symptoms - DOS), the pre-operative and two-year post-operative TAS, as well as overall TAS improvement, between patients undergoing MACI with or without a concomitant procedure. No significant differences ($p > 0.05$) were observed between the groups in any variables, so these groups were collapsed and the entire cohort was included.

Repeated measures analysis of variance (ANOVA) was initially employed to investigate the mean change in the TAS and KOOS Sport subscale across the entire cohort from pre-surgery to two years post-surgery. Furthermore, the number of patients that improved by ≥1 point on the TAS and ≥10 points on the KOOS Sport subscale over the two year period, considered as the MDCs for these measures, was reported. T-tests were employed to investigate any differences in patient demographics (age and body mass index - BMI), injury and/or surgery history (defect size and DOS) and the TAS (pre-operative TAS, post-operative TAS and overall TAS improvement) within the following group comparisons: 1) TF and PF patients, 2) patella and trochlea cases (in the PF MACI cohort), 3) males and females, 4) defect size (≤2 and >2 cm^2), 5) patient age (≤ and >40 years), and 6) those undergoing extensor realignment or not (in the PF MACI cohort). Pearson's correlations were employed to investigate the association between the TAS and KOOS Sport subscale, as well as that between the two-year post-operative TAS (and TAS improvement) and: 1) patient age, 2) defect size, 3) DOS and 4) BMI.

The level of patient satisfaction with their ability to 1) return to recreational activities and 2) participate in sport, was reported. Furthermore, the mean (SD) two-year TAS and mean (SD) TAS post-operative improvement was presented for each of the four satisfaction domains (Very Satisfied, Somewhat Satisfied, Somewhat Dissatisfied and Very Dissatisfied) across the entire cohort, and ANOVA was employed to compare the TAS among these four groups. Spearman's correlations were employed to investigate the association between the two-year post-operative

TAS (and TAS improvement) and patient satisfaction with MACI for improving the ability to undertake recreational activities and participate in sport. Statistical analysis was performed using SPSS software (SPSS, Version 19.0, SPSS Inc., USA), while statistical significance was determined at $p < 0.05$.

RESULTS

Across the entire patient cohort (inclusive of all TF and PF patients), the TAS significantly improved ($p < 0.001$) from 2.97 (SD 0.92, range 0-7) pre-surgery to 4.09 (SD 1.49, range 0-9) at two years post-surgery. A mean improvement of 1.12 (SD 1.55, range -3-6) TAS points was observed. A total of 88 patients (59%) improved ≥1 point on the TAS, including 50 TF patients (60%) and 38 PF patients (57%). Pre-surgery, a total of 136 patients (91%) reported a TAS of ≤3 points. At two years post-surgery, 85 patients (57%) scored ≥4 points on the TAS, including 46 TF patients (55%) and 39 PF patients (58%).

Across the entire patient cohort, the KOOS Sport significantly improved ($p < 0.0001$) from 27.5 (SD 23.1, range 0-95) pre-surgery to 61.1 (SD 27.3, range 0-100) at two years post-surgery. A total of 121 patients (80.7%) improved ≥10 points on the KOOS Sport subscale, including 74 TF patients (89.2%) and 47 PF patients (70.2%). A moderate though significant association ($r = 0.40$, $p < 0.0001$) existed between the improvement in the TAS and KOOS Sport, over the two year period.

In comparing patients undergoing TF and PF MACI, there were no significant differences between the groups in age ($p = 0.799$), BMI ($p = 0.901$), defect size ($p = 0.676$) and DOS ($p = 0.200$), or the pre-operative ($p = 0.455$), post-operative ($p = 0.672$) and change (0.887) in TAS (Table 3). Specifically in the PF group, patients undergoing MACI for trochlea (versus patella) lesions had significantly larger defects ($p = 0.001$); however, while both groups had similar TAS scores pre-operatively ($p = 0.918$), the trochlea MACI group had significantly better TAS scores ($p < 0.0001$) at two years post-surgery (Table 3). Furthermore, PF MACI patients that required (and hence underwent) extensor realignment surgery had significantly larger chondral defects (TTT = 3.4cm^2, no TTT = 2.7cm^2, $p = 0.020$), compared with patients that did not require realignment (Table 3). Those that underwent concomitant extensor realignment had similar pre-operative TAS scores ($p = 0.953$), though had significantly lower TAS scores ($p < 0.0001$) at two years post-surgery (Table 3).

When comparing males and females, BMI was significantly greater ($p = 0.002$) in males, though no difference was seen in all other demographic and/or surgical variables (Table 3). There was no significant difference ($p = 0.221$) in the pre-operative TAS based on gender, though males reported significantly higher TAS scores ($p < 0.0001$) at two years (Table 3). Patients > 40 years (versus ≤ 40) of age demonstrated a significantly greater DOS ($p = 0.017$) and defect size ($p = 0.008$) and, despite similar TAS scores pre-surgery ($p = 0.451$), demonstrated a significantly worse TAS score ($p < 0.0001$) at 2 years post-surgery (Table 3). While those undergoing MACI with a defect size >2cm^2 demonstrated a significantly lower ($p = 0.013$) DOS than those with a defect size ≤2cm^2, there were no other differences in patient demographics or pre- and post-operative TAS scores (Table 3). Correlations revealed that the TAS was significantly correlated with patient age (two-year TAS, $r = -0.46$, $p < 0.0001$; TAS improvement, $r = -0.35$, $p < 0.0001$) and DOS (two-year TAS, $r = -0.31$, $p < 0.0001$; TAS improvement, $r = -0.24$, $p = 0.003$), though there was no significant correlation with BMI or defect size.

Across the entire MACI cohort, 85% of patients were satisfied with the ability of MACI to improve their ability to return to recreational activities, 66% with the ability of MACI to participate in sport, and 85% were satisfied with the MACI surgery overall (Table 4). The mean TAS rating at two years post-surgery, together with the mean TAS improvement, is shown in Table 4, according to the patient's satisfaction level associated with improving the ability to return to recreational activities, improving the ability to participate in sport, and overall satisfaction level. When statistically comparing the mean two-year TAS (and TAS improvement), across the four satisfaction responses, in response to whether patients were satisfied with MACI for improving recreational activities there was no difference (two-year TAS, $p = 0.242$; TAS improvement, $p = 0.957$) between the Somewhat Satisfied (two-year TAS, mean 3.79; TAS improvement, mean 0.82) and Somewhat Dissatisfied (two-year TAS, mean 3.39; TAS improvement,

Table 3. *Patient demographics and between group comparisons: 1) Graft Location, 2) PF graft location (within the PF MACI cohort), 3) Gender, 4) Defect size, 5) Patient age, and 6) Those undergoing realignment (TTT) or not (within the PF MACI cohort).*

Group Comparison	Group	Age (y)	DOS (y)	BMI	Defect Size (cm^2)	Pre-operative Tegner	Post-operative Tegner	Tegner Improvement
Graft Location	TF	38.2 ± 11.3 (15-62)	8.4 ± 7.8 (1-26)	26.6 ± 4.0 (18.4-36.2)	3.1 ± 2.4 (0.7-10.0)	2.9 ± 1.1 (0-7)	4.0 ± 1.4 (1-8)	1.1 ± 1.6 (-3-6)
	PF	37.9 ± 11.3 (20-65)	7.3 ± 5.5 (1-21)	26.3 ± 4.3 (19.4–36.7)	3.0 ± 2.0 (0.7-12.2)	3.0 ± 0.6 (0-5)	4.1 ± 1.6 (2-9)	1.1 ± 1.5 (-1-6)
	p value	0.799	0.200	0.901	0.676	0.455	0.672	0.887
PF Graft Location	Patella	37.5 ± 11.3 (25-62)	7.8 ± 4.7 (1-18)	25.6 ± 4.4 (19.7-36.7)	2.6 ± 1.5 (0.7-6.0)	3.0 ± 0.3 (2-4)	3.8 ± 1.3 (2-7)	0.8 ± 1.3 (-1-4)
	Trochlea	38.7 ± 11.3 (20-65)	7.1 ± 6.3 (1-21)	26.7 ± 4.1 (19.4-36.0)	3.4 ± 2.5 (1.0-12.2)	3.0 ± 0.8 (0-5)	4.5 ± 1.8 (2-9)	1.5 ± 1.7 (-1-6)
	p value	0.620	0.104	0.399	0.001	0.918	<0.0001	<0.0001
Gender	Males	37.9 ± 12.1 (15-65)	7.9 ± 5.5 (1-23)	27.2 ± 3.7 (20.2-36.7)	3.3 ± 2.4 (0.7-12.2)	3.0 ± 1.0 (0-7)	4.4 ± 1.5 (1-9)	1.4 ± 1.6 (-1-6)
	Females	38.9 ± 9.7 (22-60)	8.9 ± 8.2 (1-26)	25.1 ± 4.4 (18.4-34.4)	2.9 ± 1.8 (0.7-8.0)	2.9 ± 1.0 (1-7)	3.6 ± 1.2 (2-8)	0.7 ± 1.4 (-3-6)
	p value	0.766	0.453	0.002	0.090	0.221	0.001	<0.0001
Defect Size	≤2cm^2	38.0 ± 12.3 (15-65)	10.1 ± 8.3 (1-26)	26.0 ± 4.1 (18.4-36.7)	1.4 ± 0.4 (0.7-2.0)	3.0 ± 1.1 (0-7)	4.2 ± 1.5 (3-9)	1.2 ± 1.7 (-3-6)
	>2cm^2	39.7 ± 10.3 (17-62)	7.0 ± 5.0 (1-23)	26.8 ± 4.0 (19.5-36.2)	4.7 ± 2.1 (2.2-12.2)	2.9 ± 0.8 (0-5)	4.0 ± 1.3 (1-7)	1.1 ± 1.4 (-1-5)
	p value	0.169	0.013	0.711	<0.0001	0.722	0.190	0.400
Age	≤40 y	30.0 ± 6.3 (15-39)	7.0 ± 5.8 (1-26)	26.3 ± 3.9 (19.4-36.7)	2.9 ± 2.2 (0.7-12.2)	3.1 ± 0.9 (0-7)	4.6 ± 1.6 (2-9)	1.5 ± 1.7 (-1-6)
	>40 y	48.3 ± 7.1 (41-65)	9.9 ± 7.8 (1-26)	26.4 ± 4.3 (18.4-36.2)	3.4 ± 2.3 (0.7-10.0)	2.9 ± 0.9 (0-7)	3.5 ± 1.1 (1-8)	0.7 ± 1.3 (-3-5)
	p value	<0.0001	0.017	0.829	0.008	0.451	<0.0001	<0.0001
PF MACI (with and without realignment)	PF MACI	40.3 ± 12.9 (20-65)	9.0 ± 5.4 (1-21)	25.9 ± 3.8 (19.4-36.7)	2.7 ± 2.3 (0.7-12.2)	3.0 ± 0.6 (0-5)	4.4 ± 1.7 (3-9)	1.4 ± 1.6 (0-6)
	PF MACI (with TTT)	37.2 ± 7.9 (23-49)	5.8 ± 5.1 (1-18)	26.5 ± 5.0 (19.5-33.9)	3.4 ± 1.5 (1.0-6.0)	3.0 ± 0.5 (0-5)	3.7 ± 1.4 (2-7)	0.7 ± 1.4 (-1-4)
	p value	0.111	0.001	0.741	0.020	0.953	<0.0001	<0.0001

PF= patellofemoral, MACI= Matrix-Induced Autologous Chondrocyte Implantation, TTT= tibial tubercle transfer, DOS= duration of symptoms, BMI= body mass index

mean 0.85) domains. This was also observed in response to whether patients were satisfied with MACI for improving sport participation, with no difference (two-year TAS, $p = 0.748$; TAS improvement, $p = 0.724$) between the Somewhat Satisfied (two-year TAS, mean 3.80; TAS improvement, mean 0.82) and Somewhat Dissatisfied (two-year TAS, mean 3.89; TAS improvement, mean 0.71) domains.

The two-year TAS and TAS improvement, were significantly associated with patient satisfaction in performing recreational activities (two-year TAS, rho = -0.42, $p < 0.0001$; TAS improvement, $r = -0.33$, $p < 0.0001$) and satisfaction in participating in sport (two-year TAS, rho = -0.49, $p < 0.0001$; TAS improvement, $r = -0.37$, $p < 0.0001$).

DISCUSSION

Limited research exists on exactly what level of activity patients do attain after MACI, as well as whether patients are indeed satisfied with their post-operative activity level. This study sought to primarily investigate the level of (and improvement in) activity that a community level cohort of

Table 4. *The mean Tegner Activity Scale (TAS) at two years post-surgery, together with the mean TAS improvement (pre-surgery to two years post-surgery), according to the patient's self-reported level of satisfaction for three outcomes.*

Satisfaction Question	Level of satisfaction with improving the ability to return to recreational activities?	Level of satisfaction with improving the ability to participate in sport?	Level of satisfaction with the MACI surgery overall?
Very Satisfied (n)	70	45	75
TAS (mean ± SD, range)	4.67 ± 1.75, 1-9	5.18 ± 1.79, 3-9	4.59 ± 1.71, 1-9
TAS Improvement (mean±SD, range)	1.53 ± 1.73, -3-6	1.98 ± 1.75, -3-6	1.49 ± 1.66, -3-6
Somewhat Satisfied (n)	58	54	52
TAS (mean ± SD, range)	3.79 ± 1.17, 1-9	3.80 ± 1.22, 1-7	3.83 ± 1.23, 2-7
TAS Improvement (mean±SD, range)	0.82 ± 1.33, -1-5	0.82 ± 1.39, -1-5	0.96 ± 1.41, -1-5
Somewhat Dissatisfied (n)	13	27	13
TAS (mean ± SD, range)	3.39 ± 0.87, 2-6	3.89 ± 1.22, 3-7	3.23 ± 0.83, 3-6
TAS Improvement (mean±SD, range)	0.85 ± 1.14, 0-3	0.71 ± 1.12, -1-3	0.39 ± 1.16, 0-3
Very Dissatisfied (n)	9	24	10
TAS (mean ± SD, range)	2.67 ± 0.50, 2-3	3.00 ± 0.51, 2-4	3.00 ± 0.82, 2-4
TAS Improvement (mean±SD, range)	-0.33 ± 0.50, -1-0	0.50 ± 1.18, -1-3	-0.30 ± 0.48, -1-0
Overall Satisfied (%)	85.3%	66.0%	84.7%
Overall Dissatisfied (%)	14.7%	34.0%	15.3%

MACI= Matrix-Induced Autologous Chondrocyte Implantation

patients attains at two years after MACI. Second, it sought to investigate what factors were associated with post-operative activity level, as well as whether patients were satisfied with their ability to participate in recreational and/or sporting activities. The most important finding from this study is that while a significant mean improvement was observed in the TAS and KOOS Sport as a result of MACI, only 59% of patients improved ≥1 point in the TAS and only 57% reported ≥4 points on the TAS at two years post-surgery. Despite this, 85% of patients were still satisfied with the ability of MACI to improve their ability to return to recreational activities, 66% with the ability of MACI to participate in sport, and 85% were satisfied overall with their MACI outcome.

This study employed the TAS as the activity-specific measure, with the KOOS Sport also reflecting change in sport-related tasks. A systematic review by Hambly[22] reported that 88% of cartilage repair studies demonstrated post-operative TAS improvement, though this spanned all cartilage procedures, with limited evidence specifically in MACI. The current study demonstrated a significant mean group improvement of 1.12 TAS points; however, only 59% of patients demonstrated an absolute TAS improvement (similar between TF and PF MACI), despite 81% of patients improving ≥10 points in the KOOS Sport. Furthermore, only 57% of patients reported ≥4 points on the TAS at two years, albeit the majority (91%) reported a TAS of ≤3 points before surgery. Therefore, given prior studies report mean improvement in the TAS after cartilage repair,[22] caution is required in interpreting mean improvement in the absence of data reporting individual improvement rates.

A number of factors may influence post-operative activity level. Firstly, this study did not demonstrate any difference between TF and PF MACI patients. However, while patients undergoing MACI for trochlea (versus patella) lesions specifically in the PF MACI group demonstrated significantly larger chondral defects, the trochlea MACI group actually had significantly better post-operative TAS scores, as well as overall TAS improvement. This finding was surprising, and may be related to the variation in geometry and loading of the two PF surfaces during movement. Furthermore, PF MACI patients undergoing concomitant extensor realignment surgery demonstrated significantly larger chondral defects, compared with patients that were deemed to have normal alignment undergoing MACI in isolation for PF cartilage lesions, and also demonstrated an inferior improvement in the post-operative TAS. The evidence is mixed when evaluating the effect that prior and/or concomitant surgery (i.e. ligamentous and/or meniscal repair, TF or PF re-alignment) has on post-operative activity level and RTS, when performed in combination with a cartilage repair procedure.[7,23,24] A recent study reported similar clinical and radiological outcomes in patients undergoing TF and PF MACI (only Level 3 evidence), though it did not report pre- and post-operative activity.[21]

Generally, younger patients have a higher likelihood of returning to sports[9] and, as expected, the TAS was significantly correlated with age in the current study, with patients ≤40 years of age demonstrating better post-operative TAS scores and TAS improvement, compared with those >40 years. While no association was observed between activity and BMI (or graft size), Pestka et al.[25] reported that 73% of patients returned to sport after chondrocyte implantation, though neither defect location nor graft size were associated with the return to physical activity. While the pre-operative TAS did not differ based on gender, largely as a result of patients being evaluated in their symptomatic state, males reported significantly higher TAS scores at two years. However, DOS in this study was significantly correlated with activity. Mithoefer et al.[23,24] reported that the pre-operative DOS did influence the rate of RTS in an athletic population. They further demonstrated that patients with a longer DOS had significantly lower TAS scores post-operatively. This is in contrary to Zak et al.[7] However, these studies appeared to stratify DOS by either < or > 12 months. This may be fine if the maximum DOS is two to three years in which activity level may not change too much for even a healthy unaffected active individual, though recalling activity over a longer time frame may prove difficult for many, while expecting activity level not to naturally change over five years or more, which is often unrelated to health (rather work, family etc.), is likely unrealistic. Therefore, in MACI patients it may not be appropriate to compare pre-injury to post-operative active level in patients with a longer DOS as reported in this study (the mean DOS in this study was 8.3 years and 7.3 years for TF and PF MACI patients, respectively).

Research reporting return to activity and/or sport rates after MACI is limited. After a range of cartilage repair procedures (osteochondral autograft and allografts, chondrocyte implantation and microfracture), 75-89% of patients returned to sports participation though this systematic review was undertaken in athletes.[10] A more recent meta-analysis by Krych et al.[11] also reported that overall 76% of patients RTS at mid-term follow up after cartilage restoration surgery, ranging from 58% (microfracture) to 93% (osteochondral autograft). Particularly in a community-level patient cohort (as opposed to professional athletes), a range of factors will affect post-operative activity level above and beyond ongoing knee problems, including family and work commitments, as well as other musculoskeletal and health concerns. Erdle et al.[26] recently reported that the pre-morbid level of sporting and recreational activities cannot be achieved at a minimum of 10 years after first-generation chondrocyte implantation, though they did not inquire as to when patients altered their post-operative activity, nor the reasons behind this. The current study did not evaluate other factors that can contribute to post-operative activity, though these reasons for not attaining a higher activity profile must be acknowledged. This study therefore aimed to not only evaluate the actual post-operative activity level, rather it also assessed each individual patient's level of satisfaction with what they could do, which may take into account these other factors not otherwise evaluated.

In this study, the TAS was associated with patient satisfaction in both performing recreational activities and participating in sport. However, while 59% of patients in this study reported an improvement in the post-operative TAS as a result of surgery, 85% of patients were still satisfied with the ability of MACI to improve their ability to return to recreational activities, and 66% with their ability to participate in sport. This discrepancy may highlight the aforementioned issue in employing the TAS itself, whereby patients may be able to participate in a higher level of activity, rather they have reduced this due to other reasons. This may also provide rationale for the difference in the percentage of patients surpassing the MDC in the TAS (≥1 point, 59%) and KOOS Sport (≥10 points, 81%) in the current study, whereby the TAS requires patients to report their current activity level, though the KOOS Sport requires patients to report their level of difficulty in performing sport-related tasks. It was interesting to note that when comparing the groups who were either Somewhat Satisfied or Somewhat Dissatisfied with their ability to undertake recreational activities and/or sport, no group difference in the TAS existed. This would again suggest that there are other factors that will influence the patient's perceived satisfaction toward their ability to be active.

Some limitations are acknowledged in this study. Firstly, this study employed the TAS as its activity-specific score. The TAS does not evaluate the reason for change in activity that may be unrelated to the knee, and other activity scales such as the Noyes Activity Score[27] could be considered in future research. Secondly, it did not assess the actual time to return to particular activities or sports, nor the level of pre-injury activity level, rather only activity level (and associated restrictions) when symptomatic. Therefore, this study cannot report on whether patients returned to their pre-injury activity levels; only that patients improved from their symptomatic state as a result of surgery, and whether or not they were satisfied with this post-operative level. Again, evaluating pre-injury activity is difficult in MACI patients given the often lengthy DOS (as seen in this patient cohort), unlike those who may undergo ACL reconstruction almost immediately after an acute ACL injury.

Thirdly, almost 27% of patients in this sample underwent MACI concomitantly with another surgical procedure. While this can be seen as a limitation, a patient sample undergoing various concomitant surgeries is also a strength given this study sought to evaluate a community level cohort of patients who often undergo MACI in combination with a range of other procedures. A preliminary statistical analysis also demonstrated no differences in patient factors or TAS outcomes between those undergoing MACI alone or combined with another procedure. Furthermore, we acknowledge the range of defect sizes, and that smaller lesions may be amenable to alternative procedures such as microfracture. However, MACI was the preferred method of the treating surgeons referring patients for the research program. Finally, given this was a large cohort of patients undergoing MACI for symptomatic knee cartilage defects, the group was heterogeneous with respect to graft size and location, concomitant procedures, patient age and other demographical parameters, diligence in rehabilitation, pre-operative activity/sport level and activity level desired post-surgery. However, this also presents a study strength, given it aimed to report on post-operative activity level (and satisfaction with) in a community-level cohort of patients undergoing MACI, as opposed to an elite group of athletes.

CONCLUSION

The TAS and KOOS Sport significantly improved in patients two years after MACI, though only 59% of patients improved ≥1 TAS point. Despite this, 85% and 66% of patients were satisfied with their ability to return to recreational activities and participate in sport, respectively. Age, DOS and gender were associated with post-operative activity. These findings can be used to provide realistic activity expectations to patients undergoing MACI.

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